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Title: Cleaning products and respiratory health outcomes in occupational cleaners: a systematic review and meta-analysis.

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1. What is already known about this subject?
There is consistent evidence of increased respiratory symptoms in occupational cleaners worldwide. However, uncertainty remains on type of respiratory health effects, underlying causal agents, mechanisms, and respiratory phenotypes.

2. What are the new findings?
We evaluated a broad range of respiratory health effects and estimated a 50% increased risk of asthma and 43% of COPD among occupational cleaners. No evidence for a typical allergic respiratory phenotype emerged suggesting that continuous exposure to irritant agents might cause both reversible and irreversible airway obstruction.

3. How might this impact on policy or clinical practice in the foreseeable future?
Enhanced exposure control, and respiratory health surveillance among cleaners is warranted to avoid the associated respiratory health burden. All studies lacked quantitative exposure assessment to cleaning products; inclusion of such measures in prospective studies would help elucidate underlying causal agents and mechanisms.

ABSTRACT

Objectives There is consistent evidence of increased respiratory symptoms in occupational cleaners; however, uncertainty remains on type of respiratory health effects, underlying causal agents, mechanisms, and respiratory phenotypes. We aimed to conduct a systematic review and if possible, a meta-analysis of the available literature to characterise and quantify the cleaning-related respiratory health effects.

Methods We searched MEDLINE and EMBASE databases and included studies that evaluated the association of any respiratory health outcome with exposure to cleaning occupation or products in occupational cleaners. A modified GRADE was used to appraise the quality of included studies.

Results We retrieved 1,124 articles, and after applying our inclusion criteria, 39 were selected for the systematic review. We performed a meta-analysis of the 21 studies evaluating asthma which showed a 50% increased pooled relative risk in cleaners (meta-RR= 1.50; 95%CI: 1.44-1.56). Population-based cross-sectional studies showed more stable associations with asthma risk. No evidence of atopic asthma as dominant phenotype emerged. Also, we estimated a 43% increased risk (meta-RR= 1.43; 95%CI: 1.31-1.56) of chronic obstructive pulmonary disease. Evidence for associations with bronchial-hyper-responsiveness, lung function decline, rhinitis, upper and lower respiratory tract symptoms was weaker.

Conclusions In our systematic review and meta-analysis we found that working as a cleaner is associated with an increased risk of reversible and even irreversible obstructive airway diseases. All studies lacked quantitative exposure assessment to cleaning products; this would help elucidate underlying causal agents and mechanisms. Exposure control, and respiratory surveillance among cleaners is warranted to prevent the associated respiratory health burden.

PROSPERO registration number - CRD4201705915

Keywords: respiratory health; cleaning; occupational epidemiology; public health.

INTRODUCTION

Occupational cleaners represent a significant proportion of the workforce in developed countries (about 4 million just in Europe), and mostly include 'vulnerable' social categories: women, migrants, and low educated subjects.[1] These figures are likely an underestimation given that many in this job sector are self-employed.

In the last decade, a consistent and growing evidence of an epidemic of 'asthma-like' respiratory symptoms among occupational cleaners has been reported worldwide.[2 3] In addition, a recent large population-based study found an increased risk of spirometrically-defined chronic obstructive pulmonary disease (COPD) among cleaners, confirmed in never-smokers.[4]

Cleaners are exposed to a wide range of airborne agents that might contain either respiratory sensitizers or irritants.[5 6] In particular, bleach and disinfectants have been associated with an increased asthma risk. However, most of the evidence is based on self-reported exposure that is likely to be biased towards cleaning agents with pungent odour so the causal agents remain unclear.[7]

In addition, the underlying mechanistic pathways are uncertain. There is no evidence of a classic IgE-mediated allergic asthma phenotype, so alternative pathways ranging from inflammatory to neurogenic have been proposed. Moreover, it is still largely debated whether persistent exposure to irritant agents in cleaning products could trigger and then sustain chronic airway inflammation with subsequent fixed airway obstruction.[5 6]

Given the uncertainty of causal agents, underlying mechanisms, and type of respiratory health effects, we aimed to conduct a broad systematic review and if applicable a meta-analysis of the literature in order to characterise and quantify the respiratory health effects attributable to occupational exposure to cleaning products.

This is an important public health issue, also for the potentially important downstream implications for all end-users of cleaning products during domestic housekeeping, including vulnerable 'bystanders' such as children.

METHODS

Literature search strategy, selection criteria, and quality appraisal

We conducted the systematic review following the PRISMA guidelines, and we registered the search protocol in PROSPERO (CRD42017059150) on the 21/03/17. We searched the electronic bibliographic databases "Ovid MEDLINE(R) 1946 to 2017" (PubMed) and "Embase 1947 to 2017" on the 24th March 2017. The search was then updated to the 31st July 2020. OpenGrey database was also screened to retrieve "grey literature" using broad, concise search terms covering the domains of 'Occupational cleaning' and 'Respiratory outcomes'. The search strategy used free-text terms which were adapted for each database in combination with 'MeSH' filters where appropriate (table S1 in the online supplementary file). All studies examining occupational cleaning and exposure to cleaning products including disinfectants as the exposure and any respiratory disease, symptom or lung function measure as an outcome were eligible for inclusion. Of note, "cleaning products" is used throughout this paper to designate the broader category of cleaning products and disinfectants. Healthcare workers performing cleaning job tasks were also included. To maximise the number of articles there were no restrictions on the publication date, and PhD theses captured by the grey literature search were also included. Only articles written in English were included. Case reports, editorials, letters, and reviews were excluded. Finally, studies on outdoor cleaners (e.g. road cleaners) and cleaners working in industrial/factory settings were excluded as they were likely to have been exposed at workplace to other occupational respiratory toxicants (e.g. isocyanates, food respiratory allergens, welding fumes, metals, gas, dusts, diesel exhausts, etc.) or to use cleaning agents specific for industrial applications (e.g. highly alkaline detergents for heavy industrial soiling). The full list of inclusion/exclusion criteria is in table S2 in the online supplementary file. Two authors (OA and SS) independently assessed the retrieved references against the inclusion criteria, and in case of disagreement, consensus was achieved by consulting a third reviewer (SDM). Endnote X7.1 was used as reference

management software. Given that virtually the entire evidence in occupational epidemiology comes from observational studies, a modified GRADE system [8] was used for the quality appraisal of the included articles. In particular, we considered 'a priori' as the best study design to assess a causal association a prospective observational cohort instead of a randomized clinical trial because not applicable in this occupational epidemiology context. All the other GRADE criteria were kept as per the original system, including the final scoring classification into high, moderate, low or very low.

Statistical methods for meta-analysis

To quantify the cleaning-related respiratory health effects, we considered for meta-analyses the studies included in the systematic review that showed a high/moderate quality according to the GRADE scoring. We pooled the main reported effect measures between occupational exposure to cleaning products or cleaning occupation and each respiratory health outcome by using fixed- [9] or random-effects methods [10] as appropriate based on the Higgins I^2 statistic. Significant within-studies heterogeneity is typically considered to be present if I^2 is ≥50%.[11] Also, subgroup analyses by epidemiological study type were performed. Pooled risk effect estimates were presented as meta-relative risks (RRs) and 95%confidence intervals (Cis). The meta-analysis was performed using the command 'metan' in the statistical software STATA v. 15.

RESULTS

From our electronic database search, 1,124 articles were retrieved. After removing record duplicates, 712 articles remained eligible for title and abstract screening. Of note, from forward and backward referencing of the removed review articles we identified three additional records. After abstracts screening, 148 articles remained eligible for full-text article review. After applying our inclusion/exclusion criteria, 39 studies remained to be included in the final qualitative synthesis (figure 1).

Based on our quality appraisal, most of the studies included reached a moderate GRADE score (tables S3-S5 in the online supplementary file), the three studies included that were retrieved using OpenGrey scored very low in quality and we decided to not include them in the final systematic review (tables S6 in the online supplementary file).

We managed to perform a quantitative meta-analysis among 21 high/moderate quality studies evaluating asthma risk and three high quality studies on COPD risk with comparable effect measures (figure 2, and 3, respectively). For the other evaluated outcomes, important differences in both exposure and outcome definition (e.g. bronchial-hyper-responsiveness (BHR) defined using self-reported symptoms vs. standard methacholine challenge test) prevented us from pooling these studies in a meta-analysis.

Respiratory health outcomes

Asthma

We included in the systematic review 21 studies evaluating associations between asthma and occupational cleaning (and/or exposure to cleaning products) conducted in a broad range of countries (Europe, USA, South America, Canada, and New Zealand) in the last two decades (table 1). Thirteen studies were based on general population samples, [12-24] and eight were conducted within workforces.[25-32] The majority used a cross-sectional design. In terms of outcome definition, 'adult-onset asthma' among current or ever cleaners was mainly used as a *proxy* to define 'occupational asthma' or the broader category of 'work-related asthma' outcomes, based on a self-reported doctor's diagnosis or asthma symptoms/medications. Of note, studies evaluating work-exacerbated asthma only, were not included. Most of the studies used a standard job-title approach as *proxy* for occupational exposure to cleaning products. Six studies assessed exposure to specific agents included in cleaning products by using an expert-based exposure assessment or a semi-quantitative job-exposure matrix (JEM)

approach. [13 17 18 26 27 33] Evidence of a positive exposure-response relationship emerged by using duration of employment as a cleaner or frequency/intensity/duration of cleaning tasks as *proxys* for exposure. Most of these studies were conducted among hospital cleaners and evaluated frequency and intensity of exposure to disinfectants during cleaning tasks [21 25-27] None actually managed to measure cleaners' personal exposure to cleaning agents, so no dose-responses based on concentration metrics were evaluated. Both population- and workforce-based studies found a positive association between occupational cleaning and asthma risk. Among the eight workforce-based studies, [25-32] mainly conducted among hospital healthcare workers, risk estimates were more instable because based on smaller samples. Of note, among healthcare workers emerged positive exposure-response trends for asthma risk and exacerbations for frequency of cleaning tasks, especially when applying disinfectants/sterilising agents. [25] Exposures to ammonia and bleach showed the highest associations with asthma risk both in workforce-, and population-based studies. [19 20] Also, cleaning products in spray format were found more strongly associated with asthma symptoms or asthma exacerbations compared to liquid and powder products. Of note, we did not include in the systematic review a French population-based case-control study that evaluated asthma severity only [33] and a cross-sectional study of cleaners in Brazil because a composite outcome of asthma/rhinitis symptoms was evaluated.[34]

Meta-analysis for asthma outcome

Based on our GRADE quality appraisal (table S3 in the online supplementary file), we selected 21 studies on asthma with high/moderate quality score for meta-analysis.

Where studies reported more than one risk effect estimate for asthma, we selected for quantitative summary the one that best-defined occupational asthma: for example, we favoured the effect estimate for asthma diagnosis after start work among current cleaners over estimates for ever adult asthma diagnosis among ever cleaners.

The population-based studies showed a clear increased risk of asthma among cleaners, irrespective of the study design, with the highest pooled risk estimate among cross-sectional studies (meta-RR= 1.53; 95%CI: 1.36-1.72). Workforce studies found positive, but less stable associations (i.e. wider confidence intervals), with the highest pooled risk among cross-sectional studies (meta-RR= 1.76; 95%CI: 1.33-2.34).

Overall, the pooled meta-analysis of the 21 studies, showed a 50% increased risk for asthma (meta-RR= 1.50; 95%CI: 1.44-1.56; I^2=33.7%; p=0.07) (figure 2). Based on the heterogeneity tests between studies, fixed methods were applied to pool the risk estimates.

No evidence of publication bias or small-study effects was detected (Egger's test p =0.23) (figure S1 in the online supplementary file).

Bronchial hyper-responsiveness (BHR)

Among the three studies included in the systematic review that evaluated non-specific BHR as respiratory outcome among occupational cleaners a weak positive association was found (table 2). [23 26 35] In particular, only one study found a clear association with BHR even if assessed using a symptoms score questionnaire instead of an objective a specific bronchial challenge test.[26] One study found an association in ex-smokers only,[22] and one did not find a statistically significant association. [35] Two studies included in the systematic review were not included in table 2 because evaluated BHR only in a combined outcome with asthma symptoms. [16 22]

Respiratory symptoms

Eleven studies (five workforce and six population based) investigated as outcomes lower (LRTS) and upper (URTS) respiratory tract symptoms, such as cough, wheeze, or chest tightness, and itchy, or runny nose, respectively (table 2). [21 24 29 30 35-41] Eight of the eleven studies explored only LRTS and found an increased risk for higher duration of exposure and among those working as cleaners compared to controls. In one study this increased risk was confined to women although no formal gender interaction was tested,[29] while in another study there was evidence of a positive exposure-response (OR of wheeze of 1.46; 95%CI: 1.18–

1.83 for exposure between one and 4 years; and of 1.62 (95%CI: 1.34–1.96) for exposure >4 years.[21] One cross-sectional study in Spain showed increased risk of LRTS in cleaners, but failed to reach conventional statistical significance.[30] Finally, one study found a significant increase in phlegm (p=0.019) and dyspnoea (p=0.041) suggestive for chronic bronchitis.[35] Three studies assessed also associations with URTS. One study showed a doubled risk for eye/nose/throat symptoms;[40] the second found associations confined only to medium and not high exposures which were attributed by the authors to the healthy worker effect.[36] The third found a significant increase in nasal (p<0.001) and throat symptoms (p<0.05).[38]

Rhinitis

Two population-based studies reported the association of cleaning profession with occupational rhinitis as outcome [19 42] and one workforce-based assessed associations with the composite outcome rhinitis/asthma [34] (table 3); most have shown small and statistically not significant increased risks. Phenotypes of rhinitis were examined by one study that found increased risk of perennial rhinitis among cleaners, especially women (OR=1.70 (1.09 to 2.64).[42] Similarly in Brazil, female cleaners only had higher risk of a composite outcome rhinitis/asthma (rhinitis defined as self-reported sneezing or runny or blocked nose, without cold or flu over the past 12 months).[34] Neither of these studies conducted formal tests for gender interaction. Evidence from a cross-sectional study in Spain on current and former cleaners (domestic and non-domestic) showed increased and significant associations with rhinitis only for former domestic cleaners).[19]

COPD

Three studies examined the association between occupational cleaning exposure and COPD risk.[4 21 43] A significant association of working as a cleaner and having spirometrically-defined COPD (i.e. forced expiratory volume in one second, FEV_1/forced vital capacity, FVC < lower limit of normal, LLN) was found in a recent large population-based cross-sectional analysis of 228,614 people in the UK Biobank study. A 43% risk increase (prevalence ratio, PR=1.43;95%CI:1.28-1.59) was found for cleaning occupation, also confirmed in analyses restricted to never smokers, and non-asthmatics.[4] Also, a cross-sectional study of 13,499 Northern European cleaners reported an increased risk of self-reported COPD diagnosis (OR=1.69; 95%CI: 1.29–2.20)[21]. Finally, a very recent workforce-based prospective cohort study among hospital nurses in US found an increased incidence of COPD (self-reported doctor-diagnosis) for exposure to cleaning products and disinfectants (Hazard Ratio (HR)=1.35; 95%CI: 1.14-1.59) for weekly self-reported exposure to any disinfectant) [43] (table 3).

Meta-analysis for COPD outcome

Overall, the pooled meta-analysis of these three studies,[4 21 43] showed a 43% increased risk for COPD (meta-RR= 1.43; 95%CI: 1.31-1.56; I^2=0.0%; p=0.38) (figure 3). Based on the heterogeneity tests between studies, fixed methods were applied to pool the risk estimates. No evidence of publication bias was detected (Egger's test p =0. 60) (figure S2 in the online supplementary file).

Lung function metrics

Seven studies (table 3) evaluated as outcome lung function metrics decline in occupational cleaners.[23 31 37 44-47] The majority did not find significant differences in lung function among cleaners compared to controls. For example, one large multicentre population-based study found a significant decrease of cross-shift peak expiratory flow (PEF) only [23], and another found lower cross-shift FEV1, and PEF among cleaners with current asthma only. [45] However, a recent international population-based longitudinal study found an accelerated lung function decline among professional cleaners (FEV1: -22.4ml/year; p = 0.03, and FVC: -15.9ml/year; p = 0.002).[47] Also, a very recent workforce-based cross-sectional study in New

Zealand found a significant decline in lung function metrics among cleaners compared to controls.[31]

Other health outcomes

Among other health outcomes evaluated to better clinically phenotype the specific respiratory health effects among cleaners, atopy has been the one mostly investigated, not only because asthma is commonly allergy-based, but also because cleaning products often contain potent IgE-mediated sensitising agents such as chloramine-T, ortho-phthalaldehyde and enzymes. One large multinational study showed a lower prevalence of atopy in cleaners compared to office workers (38.3% vs. 60.9%; $p<0.05$).[23] Of note, a workforce case-control study found higher atopy in cleaners with asthma than without (42% vs. 10%, respectively), also associated with higher total IgE serum levels (geometric mean ratio: 2.9; 1.5-5.6). [46]

Fractionated exhaled nitric oxide (FeNO), a marker of airways inflammation and eosinophilic infiltration that has been associated with atopic asthma, has also been investigated. Three studies investigating FeNO in exhaled breath condensate after acute (pre- vs. post-shift) exposure to cleaning products containing chlorine did not found a significant difference between cleaners and controls.[44 46 48] Of note, in one of them, a positive association of exposure to cleaning products with biomarkers of oxidative stress and inflammation (i.e. Malondialdehyde (MDA), 4-hydroxynonenal (4-HNE), Nitrates (NO3-), in the exhaled breath condensate was found [48] (table 3).

Grey literature

As above stated, the three studies included from searching the OpenGrey database were excluded from the final systematic review because of the low quality or missing information to assess the GRADE scoring (table S6 in the online supplementary file).

Briefly, one very small workforce surveillance study found increased asthma prevalence diagnosed via PEF diary among hospital cleaners.[49] Another workforce survey found a non-significant higher prevalence of self-reported asthma and chronic bronchitis among hospital cleaners compared to administrative controls.[50] A small population cross-sectional study showed a higher prevalence of BHR (based on histamine challenge test) and associated respiratory symptoms (e.g. cough, phlegm, wheezing) compared to office workers.[51]

DISCUSSION

Our systematic review examined for the first time a broad variety of respiratory health effects in association with occupational exposure to cleaning products.

We found a clear increased risk of asthma among occupational cleaners, that we quantified by performing a meta-analysis into 50%. Of note, the majority (15 out of 21) of the studies included in the meta-analysis used cleaning occupation as a *proxy* for occupational exposure to cleaning agents, and therefore were not susceptible to recall bias. Most of the studies were cross-sectional by design, and evaluated asthma as self-reported doctor's diagnosis, or asthma symptoms; only a few managed to assess it by objective lung function tests. Also, supporting positive exposure-relationship by duration of employment or exposure (mainly self-reported) to cleaning agents were found.

Weaker positive associations were found for BHR, LRTS, and URTS, and rhinitis. In particular, BHR was increased among cleaners although within individual studies this rarely reached conventional levels of statistical significance. Among the LRTS assessed, chronic cough and wheezing were reported as increased among cleaners, often when evaluated in association with an asthma diagnosis. Among the URTS, a weaker, but interesting, association with inspiratory breathing suggestive for irritant vocal cord dysfunction was found. Also, rhinitis was inconstantly found increased among cleaners, and only when associated to exposure to high molecular weight allergens in cleaning agents.

Interestingly, the majority of studies did not find an association with single lung function metrics as outcomes, namely FEV1, FVC, and FEV1/FVC ratio. This is maybe due to well-known low

sensitivity of occasional spirometry tests to detect occupational asthma or suggesting that if asthma-like symptoms arise in cleaners, it may not be due to airway obstruction but to other underlying mechanisms. Of note, a recent international population-based longitudinal study reported significant lung function decline associated with cleaning work that would support long-term respiratory health-effects.[47]

In addition, we found an increased COPD risk for cleaning occupation, that we managed to quantify into 43% based on three high quality large population-based studies. It is noteworthy that the largest of the two used a spirometry-based definition of COPD and managed to confirm these findings in both never smokers, and non-asthmatics, so ruling out residual confounding by both tobacco and asthma. This result is important because COPD has been largely linked to other occupational exposures such as generic VGDF (i.e. vapour, gas, dust, fumes) exposure, but the evidence for cleaning agents is still scarce.

In relation to the potential associated respiratory phenotypes, no clear association with allergy, or exhaled FeNO (i.e. biomarker of airway inflammation in asthma patients) was found, but an association with biomarkers of oxidative stress and inflammation (i.e. MDA, 4-HNE, and $NO3^-$) was reported.

Among the evaluated potential causal agents, chlorine-based cleaning products, such as bleach were found associated with increased asthma risk,[37] but also ammonia, quaternary ammonium compounds, disinfectants and sterilising agents such as ethanolammide, and glutaraldehyde, especially among healthcare workers performing cleaning tasks.[27] As expected, cleaning products in spray format were associated with an higher asthma risk. [22] Nevertheless, the lack of personal quantitative exposure assessment to the above agents and their pungent odour make these findings potentially susceptible to recall bias.

Overall, our findings seem to support the still debated hypothesis that cleaning-related respiratory health effects may be caused via irritation- rather than immuno-mediated underlying mechanisms. As previously suggested, [52] chronic exposure at relatively moderate doses, such as among occupational cleaners, to airborne irritative chemicals could cause inflammation and subsequent bronchoconstriction. Also, our results suggest that if exposure at work to noxious cleaning agents persists a reversible airway obstruction could become irreversible. This is confirmed by studies included in this review that found a positive exposure-response relationship by employment duration and frequency/intensity of exposure to cleaning-tasks.[21 25-27]

Our systematic review has several strengths. It evaluated a broad range of respiratory health effects and associated phenotypes, and it aimed to be very comprehensive by including also grey literature, as confirmed by the absence of publication bias. Also, we evaluated the evidence quality by applying a standard quality scoring system slightly modified to be suitable to appraise occupational epidemiology evidence. Finally, we managed to quantify a pooled risk estimate for asthma and COPD outcomes that can be used to inform public health interventions, and future similar studies on the topic.

Limitations include the exclusion of articles not in English language. Also, misclassification of both exposure, and outcome, cannot be ruled out, and not all studies adjusted for the same potential confounders. However, both the meta-analysis for asthma and COPD outcomes among the selected studies showed a low heterogeneity that allowed us to use fixed-effect pooling methods.

In conclusion, in our systematic review we found that occupational exposure to cleaning product is associated with several respiratory health effects, including both reversible and irreversible airway obstruction, and the suggested causal association is supported by evidence of positive exposure-response trends.

These findings have important potential public health implications: preventive measures to avoid, or at least reduce exposure to cleaning agents at workplace should be implemented, and respiratory health surveillance should be strengthened among this category of workers in order to detect early signs of respiratory health effects, and so avoid any subsequent morbidity and disability. In addition, according to the precautionary principle, important downstream implications for all end-users of cleaning products during domestic housekeeping, could be to suggest reducing exposures to ‘as low as possible’, especially to protect vulnerable subjects

such as children from potentially harmful 'bystander' exposure. Our findings are particularly relevant in the current COVID-19 pandemic. Use and exposure to cleaning products in the general population has globally increased for infection control. We recommend adding to pandemic guidance documents information on cleaning-related respiratory health effects and on safe use of cleaning products to prevent the associated public health burden.
Further studies, ideally prospective cohorts using more precise quantitative exposure assessment of individual cleaning agents (e.g. exact chemical composition by use of product bar codes), detailed clinical phenotyping (e.g. airway inflammatory and immune biomarkers), and modern molecular methods (e.g. metabolomics), would help clarify both the underlying causal agents, and the relevant biological mechanisms. Filling this knowledge gap would allow implementation of effective focussed preventive intervention strategies aimed to eliminate or at least control exposure to hazardous cleaning agents and identify early health effects to prevent the associated occupational respiratory health burden with important personal, medical and societal benefits.

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Contributors SS and OA performed the literature review. SDM and DJ designed the project. SDM performed the meta-analyses. DC performed the literature search update and related tables' amendments. SDM, OA, DC and DJ, revised and approved the manuscript.

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Table 1: Summary of epidemiological studies (chronological order) assessing the associations between cleaning occupation, tasks, or agents and asthma in population- and workforce-based studies

Author, year	Country	Period of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Kogevinas, 1999	26 centres in 12 countries	1992	Population-based survey (ECRHS)	15,637 people randomly selected from the general population (n=443 cleaners)	Asthma was assessed by methacholine challenge test and questionnaire	Age, sex, smoking status, study centre	Cleaning occupation	BHR and asthma symptoms or medications: OR=1.97 (1.33-2.92) Asthma symptoms or medication: OR=1.82 (1.44-2.30)	Medium
Zock, 2001	Spain	1998	Population-based cross-sectional (ECRHS)	67 indoor cleaners, 1,272 office workers	Questionnaire, blood samples for serum IgE	Age, gender, smoking, study centre	Confirmed cleaners	BHR and asthma symptoms or medications: OR=2.8 (1.3-6.2) Asthma symptoms or medication: OR=1.7 (1.1-2.6) Higher PRs for private home cleaners	Moderate
Karjalainen, 2002	Finland	1986-1998	Registry-based cohort	53,708 cleaners, 202,751 administrative managerial and clerical workers	The Medication Reimbursement Register of the SII of Finland and the Finnish Register of Occupational Diseases (FROD)	Age, follow-up period	Female cleaners	WRA: RR=1.50 (1.43 -1.57)	High
Zock, 2002	11 European countries and 3 outside Europe	1990-1994	Population-based survey (ECRHS Stage II)	304 cleaners, 4,492 office workers	Questionnaire, blood samples for serum IgE	Age, gender, smoking, study centre	Cleaning occupation	Current asthma OR=2.47 (1.7-3.6)	Moderate
Jaakkola, 2003	Finland	1997-2000	Population-based case-control	521 asthma cases, 932 controls	Questionnaire	Age, gender, smoking	Female cleaners	OA: OR=1.42 (0.81-2.48)	Moderate
Medina-Ramón, 2003	Spain	2000-2001	Population-based cross-sectional	4,521 female domestic cleaners, 593 current, 1170 former	Questionnaire	Age, smoking	Current and former cleaning	Ever cleaning for current asthma: OR=1.73 (1.44-2.07) Current cleaner for current asthma: OR=1.32 (1.04-1.69) Current cleaner for current asthma (domestic only) : OR=1.46 (1.10-1.92) Former cleaner for current asthma: OR= 2.00 (1.63 to 2.43)	High

Author, year	Country	Period of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Le Moual, 2004	France	1975	Population-based survey	404 cleaners, 8,428 administrative service workers	Questionnaire ISCO-88 JEM	Age, gender, smoking	Cleaning occupation Generic asthmagens	WRA, cleaning job: OR=1.04 (0.70-1.54) WRA, cleaning agents: OR=2.16 (1.12-4.17)	Moderate
Delclos, 2007	US	2003	Workforce based cross-sectional	3,650 healthcare professionals (862 physicians, 941 nurses, 968 occupational therapists, 879 respiratory therapists)	Questionnaire	Age, sex, race/ethnicity, professional group, years as a health professional ("seniority"), smoking, obesity	Exposure to cleaning agents/tasks Seniority: 10-16 years 17-26 years ≥27 years	WRA Medical instrument cleaning: OR=2.22 (1.34-3.67) General cleaning: OR=2.02 (1.20-3.40) Use of powdered latex gloves between 1992 and 2000: OR=2.17 (1.27-3.73) Administration of aerosolized medications: OR=1.72 (1.05-2.83) OR=2.08 (0.64-6.73) OR=3.37 (1.10-10.26) OR=4.10 (1.39-12.11)	High
Kogevinas, 2007	13 countries	1998-2003	Population-based cohort (ECRHS-II)	6,837 (358 of them cleaners)	ECRHS II questionnaire	Age, sex, smoking, centre	Cleaning and caretaking Cleaning products using asthma-specific JEM	Cleaning and caretaking occupation: OR=1.71 (0.92-3.17) Exposure to cleaning products: OR=1.80 (1.01-3.18)	High
Mirabelli, 2007	22 centres located in 10 European countries	1998-1999	Population-based cohort (ECRHS-II)	332 nurses or employed in nursing-related job, 2,481 professional or administrative workers	Questionnaire ISCO-88	Age, country, sex, smoking, study area	Exposure to cleaning products, cleaning tasks among healthcare workers	New-onset asthma Ammonia and/or bleach: OR=2.16 (1.03-4.53) Liquid multi-use products: OR=1.16 (0.61 -2.19) Washing powders OR=1.65 (0.77-3.53) Any products in spray form OR=2.36 (0.99-5.64)	High
Obadia, 2009	Canada	Not specified	Workforce-based cross-sectional	566 cleaners and 587 other building workers	Questionnaire	Age, gender, smoking	School or racetrack public building cleaners	OA, males OR=0.93 (0.4-2.3) OA, females: OR=1.00 (0.4-2.3)	High
Eng, 2010	New Zealand	2004-2006	Population-based cross-sectional	3,055 participants (from a random sample of 10,000)	Telephone survey	Age, gender, smoking, deprivation	Cleaners	WRA, adult onset: OR=1.3 (0.8-2.1) WRA, current: OR=1.60 (1.09-2.35	Moderate

Author, year	Country	Period of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Vizcaya, 2011	Spain	2007-2008	Cross-sectional study on employees of cleaning companies	917 employees of 37 cleaning companies: 761 current cleaners, 86 former and 70 never cleaners (referents)	Spirometry during clinic visit	Age, gender, nationality. smoking status	Cleaning occupation Cleaning products	Current asthma, current cleaners: OR=1.9 (0.5-7.8), former cleaners: OR=1.9 (0.6-5.5) Adult-onset asthma, current cleaners: OR=1.4 (0.4-4.9), former cleaners: OR=2.5 (0.5-12) Use of hydrochloric acid: OR=1.7 (1.1-2.6)	Moderate
Arif and Delclos, 2012	US	2004-2005	Workforce based cross-sectional	3650 healthcare professionals	Questionnaire (exposure to cleaning substances) In the longest held job	Age, sex, race/ethnicity , BMI, seniority, atopy, smoking status	Cleaning agents	WRA symptoms increased in a dose-dependent manner from OR=2.64 (95% CI 0.57-12.1) for 1/week exposure to cleaning agents to OR=5.37 (1.43-20.16) for >1/day. For exposures to disinfectants/sterilising agents, WEA increased from 3.75 to 5.06 to 9.02 for at least 1/week, every day and more than once a day, respectively. OA for every day and >1/day self-reported exposure to cleaning agents: 0.81 (0.17-3.86)	High
Dumas, 2012	France	2003-2007	Workforce based case-control	179 hospital workers, 545 controls, selected from a previous case-control study	Questionnaires, expert assessment and the asthma JEM	Gender, BMI	Among hospital workers: frequency of cleaning tasks: (never, <1, 1-3, 4-7 days/week	In women, for exposure >1day/week (expert only): OR=1.04 (0.64-1.70); high intensity: OR=1.45 (0.81-2.62) In women, for exposure (expert+JEM) to high intensity cleaning/disinfecting tasks: OR=2.32 (1.11-4.86). Moderate/high exposure to quaternary ammonium: OR=1.93 (0.85-4.40)	High

Author, year	Country	Period of data collection	Study design	Study population	Method of data collection	Covariates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
h, 2013	Great Britain	1991-2000	Population-based cohort	Cleaners unspecified: 156 Domestic helpers and cleaners: 113 Helpers and cleaners in offices, hotels: 516	Interview	Gender, smoking, father's social class, area of residence at 42 years, hay fever/ allergic rhinitis in childhood	Domestic cleaners identified and coded using the ISCO-88 Cleaning products using asthma-specific JEM	Adult onset asthma in cleaners unspecified: OR =1.58 (0.95-2.63) Domestic helpers and cleaners: OR=1.79 (1.02-3.14) Helpers and cleaners in offices, hotels: OR=1.82 (1.34-2.48) Cleaning/disinfecting products: OR= 1.67 (1.26-2.22)	High
Gonzalez, 2014	France	2006-2007	Workforce-based cross-sectional	543 healthcare workers (94 cleaners)	Questionnaire	Age, gender, smoking, atopy, BMI	Hospital cleaners	WRA, cleaning profession: crude OR=2.38 (0.48-11.85) OA, crude OR=2.33 (0.52-10.44) General cleaning tasks: adjusted OR=2.26 (0.95-5.35)	Moderate
Svanes, 2015	Norway, Sweden, Denmark, Iceland, Estonia	2010-2012	Population-based cross-sectional (RHINE III), extension of ECRHS)	2,138 ever cleaners (from 13,499 respondents)	Questionnaire	Age, gender, smoking, educational level, parent's educational level, BMI, centre	Occupational cleaner (ever	OA OR=1.47 (1.22-1.27) Positive trend with duration of exposure	High
Abrahamsen , 2017	Norway	February to August 2013	Population-based cross-sectional study	185 cleaners (among 16,099 responders)	Questionnaire	Age, gender, area of residence, smoking, home damp/ mould, housing conditions	Female and male cleaners JEM	Current asthma: OR=1.4 (0.61-3.2) Physician diagnosed asthma (ever): OR=0.92 (0.51-1.60)	Medium
Brooks, 2020	New Zealand	2008-2010	Workforce based cross-sectional	425 cleaners, 281 reference workers	Questionnaires, bronchodilator	Age, gender, ethnicity, smoking	Cleaners	Current asthma in cleaners: OR=1.83 (1.18-2.85) Physician-diagnosed asthma ever: OR= 0.62 (0.42-0.92)	High
Dumas, 2020	US	2009-2015	Workforce based prospective cohort study (NHSII)	116,429 female registered nurses	Questionnaires	Age, smoking status and pack-years, race, ethnicity, and BMI	Disinfectants Sprays for cleaning, disinfection, other JEM	OA Exposure to any disinfectant: HR=1.12 (0.91-1.38) Weekly use of sprays: HR=1.10 (0.76-1.59)	High

ECRHS: European Community Respiratory Health Survey; HR: hazard ratio: ISCO: International Standard Classification of Occupations: JEM: job-exposure matrix; NHSII: Nurses' Health Study II; OA: occupational asthma; OR: odds ratio; PR: prevalence ratio; RHINE: respiratory health In northern Europe; WEA: work-exacerbated asthma; WRA: work-related asthma

Table 2. Summary of epidemiological studies (chronological order) assessing the associations between cleaning occupation, tasks, or agents and bronchial hyperresponsiveness (BHR) and upper (UTRS) and lower (LTRS) tract respiratory symptoms

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
BHR									
Zock, 2002	11 European countries and 3 outside Europe	1990-1994	Population-based survey (ECRHS)	304 cleaners, 4,492 office workers	Spirometry, methacholine challenge test	Age, gender, smoking, study centre	Cleaning occupation	Case-case analysis: OR =1.60 (p>0.05)	Moderate
Delclos 2007	US	2003	Workforce-based cross-sectional	3,650 healthcare professionals (862 physicians, 941 nurses, 968 occupational therapists, 879 respiratory therapists)	Questionnaire, BHR defined as 8-item, symptom-based predictor of PC20, JEM	Age, sex, race/ethnicity, professional group, years as a health professional ("seniority"), smoking, obesity	Exposure to cleaning agents/tasks	Outcome: BHR related symptoms General cleaning: OR=1.63 (1.21-2.19) Cleaning products used on building surfaces: OR=1.74 (1.34-2.26) Instrument cleaning: OR=1.40 (1.09-1.79) Adhesives/solvents/gases in patient care: OR=1.86 (1.42-2.44)	High
Karadzinska-Bislimovska 2007	FYROM	2004-2006	Cross-sectional	Women, 43 cleaners,37 cooks, 45 controls (office workers)	Questionnaire	Smoking, BMI, baseline FEV1	**Female cleaners**	Prevalence of BHR higher in cleaners than controls though not statistically significant (30.2% vs 17.7%).	Moderate
LRTS and URTS									
Nielsen and Bach, 1999	Denmark	1989-1991	Workforce-based cohort	1,011 female cleaners employed at nursing homes, schools and offices	Questionnaire	Age, smoking	Female domestic cleaners Use of sprayers	Continuous use of sprayers Eye/nose/throat symptoms: OR=2.1 (1.1-3.8) Asthma symptoms: OR=3.0 (0.9-10) Bronchitis: OR=3.2 (1.0-10.4)	Moderate

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Medina-Ramón, 2005	Spain	2001-2002	Case-control, nested within a large population-based survey	Domestic cleaning women, 40 cases (with asthma and/or chronic bronchitis symptoms, 155 controls)	Questionnaire Lung function, methacholine challenge, serum IgE testing Personal measurements of airborne chlorine and ammonia	Age, smoking, bleach, cleaning products, washing dishes, inhalation accidents, non-domestic cleaning	Female domestic cleaners	Combined outcome: asthma/chronic bronchitis symptoms Bleach use Intermediate exposure: OR=3.3 (0.9-11) High exposure: OR=4.9 (1.5-15)	Moderate
Medina-Ramón, 2006	Spain	2001-2002	Population-based cross-sectional panel	43 female domestic cleaners recruited from a previous case-control study	Diary Lung function and allergy testing	Age, respiratory infections, medications	Domestic cleaners	LRTS more common on working days: OR=3.1 (1.4-7.1) LRTS predominantly associated with exposure to diluted bleach, degreasing sprays/atomisers and air fresheners	Moderate
Karadzinska-Bislimovska, 2007	FYROM	2004-2006	Population-based cross-sectional	Women, 43 cleaners,37 cooks, 45 controls (office workers)	Questionnaire	Smoking, BMI, baseline FEV1	Female cleaners	Significantly higher prevalence of phlegm (p=0.019) and dyspnoea (p=0.041) in cleaners compared to the control group	Moderate
Obadia 2009	Canada	Not specified	Workforce-based case control	566 cleaners and 587 other building workers	Questionnaire	Age, gender, smoking	School or racetrack public building cleaners	LRTSs in female cleaners: OR=2.59 (1.6-4.3) LRTSs in male cleaners: OR 1.16 (95% CI 0.7 -1.9)	High
Wieslander and Norback, 2010	Sweden	Not specified	Population-based cross-sectional	21 hospital cleaners	Questionnaire		Hospital cleaners	Significant increase in nasal symptoms (p<0.001) and throat symptoms (p<0.05) Significant increase in dyspnoea (p<0.01)	Low

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Vizcaya 2011	Spain	2007-2008	Cross-sectional study on employees of cleaning companies	917 employees of 37 cleaning companies: 761 current cleaners, 86 former and 70 never cleaners (referents)	Spirometry during clinic visit	Sex, age, nationality, smoking status	Cleaning occupation	Wheeze without having a cold, current cleaners: OR=1.3 (9 0.5-3.3), former cleaners: OR=2.0 (0.6-6.5) Chronic cough, current cleaners: OR=1.8 (0.7-4.7), fomr cleaners: OR=1.9 (0.5-7.8)	Moderate
Lee, 2014	USA	Not specified	Workforce-based cross-sectional	183 hospital cleaners	Questionnaire, face to face interview	Age, gender, job title	Hospital cleaners. Exposure classified in tasks and cleaning products used	For chemical-related symptoms (Respiratory tract, eye, skin, nervous,and gastrointestinal systems): <u>Medium exposure</u> Cleaning tasks using sprays: OR= 3.16 (1.24-8.04) Cleaning toilet bowls or sinks: OR=1.71 (0.72-4.01) Bleach: OR= 1.29 (0.55-3.04) Disinfectants: OR= 0.67 (0.28-1.62) Liquid multi-use cleaning products: OR= 0.83 (0.35-1.95) <u>High exposure</u> Cleaning tasks using sprays OR=1.98 (0.87-4.51) Cleaning toilet bowls or sinks: OR= 1.96 (0.82-4.69) Bleach: OR= 1.68 (0.70-4.01) Disinfectants: OR=0.72 (0.30-1.74) Liquid multi-use cleaning products: OR= 2.35 (1.02-5.43)	High

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Svanes 2015	Norway, Sweden, Denmark, Iceland Estonia	2010-2012	Population-based cross-sectional (Respiratory Health In Northern Europe, part of ECRHS)	2,138 ever cleaners (from 13,499 respondents)	Questionnaire	Age, gender, smoking, educational level, parent's educational level, BMI, centre	Occupational cleaner	Wheeze last 12 months: OR=1.44 (1.27-1.62) Asthma symptoms: OR=1.66 (1.46 -1.90) Positive trend with duration of exposure for both outcomes	High
Abrahamsen 2017	Norway	February to August 2013	Population-based cross-sectional study	185 cleaners (among 16,099 responders)	Questionnaire	Age, gender, area of residence, smoking, home damp/ mould, housing conditions	Female and male cleaners JEM	Wheezing OR=0.76 (0.47-1.2) Woken with dyspnoea OR=0.63 (0.27-1.4)	Medium
Whitworth 2019	US	2017	Cross-sectional study	56 Hispanic female domestic cleaners	Questionnaire	Age and ever smoking	Cleaning tasks and agents	Exposure to cleaning tasks was statistically insignificantly associated with BHR symptoms. Exposure to ammonia: OR=7.5 (1.6-35.9). Exposure to solvents and use of sprays for air freshening was also associated with BHR related symptoms	Medium

ECRHS: European Community Respiratory Health Survey; JEM: job-exposure matrix; OR: odds ratio; PR: prevalence ratio

Table 3. Summary of epidemiological studies (chronological order) assessing the associations between cleaning occupation, tasks, or agents and rhinitis, chronic obstructive pulmonary disease (COPD), lung function, and other health outcomes

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Rhinitis									
Medina-Ramon 2003	Spain	2000-2001	Population-based cross-sectional	4,521 female domestic cleaners, 593 current, 1170 former	Questionnaire	Age, smoking	Current domestic cleaners Former domestic cleaners	Current cleaner: OR=1.08 (0.92-1.28) Former cleaner: OR=1.27 (1.12-1.47)	High
Maçãira 2007	Brazil	December 2002 to May 2003	Workforce-based cross-sectional	341 cleaners	Questionnaire, skin prick test	Age, gender, smoking, atopy, number of years employment in non-domestic cleaning, inhalation accidents	Employment in non-domestic cleaning: 0.92-3 years 3-6.5 years >6.5 years	 WRA/rhinitis OR=1.09 (1.00-1.18) WRA/rhinitis OR=1.28 (1.01-1.63 WRA/rhinitis OR=1.71 (1.02-2.89	Moderate
Radon 2008	Europe, 27 centres	1998-2003	Population-based cohort study (ECRHS II)	4.994 (294 of them Cleaners and caretakers)	Face-to-face interviews	Country, age at first survey, smoking, parental allergies, level of education	Occupations, asthmagens JEM	New-onset allergic rhinitis, cleaners and caretakers: OR=1.25 (0.86-1.81) Perennial rhinitis, cleaners and caretakers: OR=1.43 (0.99-2.06).	High
COPD									
Svanes 2015	Norway, Sweden, Denmark, Iceland, Estonia	2010-2012	Population-based cross-sectional (Respiratory Health In Northern Europe, part of ECRHS)	2,138 ever cleaners (from 13,499 respondents)	Questionnaire	Age, gender, smoking, educational level, parent's educational level, BMI, centre	Occupational cleaner (ever) Duration of exposure: ≤1 year 1-4 years ≥4 years	Self-reported COPD: OR=1.69 [1.29-2.20] OR=1.41 (0.85-2.33) OR=1.80 (1.14-2.85) OR=1.65 (1.14-2.42)	High

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
De Matteis 2016	UK	2006-2010	Population-based cross-sectional (within the Biobank Cohort)	228,614 participants adults, 2017 cleaners	Self-administered questionnaires, face-to-face interviews and physical health measurements	Sex, age, recruitment centre, lifetime tobacco smoking	Domestic cleaners	COPD defined as FEV1/FVC<LLN) PR=1.43 (1.28 1.59) Never smokers: PR=1.38 (1.15 1.66) Non-asthmatics: PR=1.46 (1.29 1.65)	High
Dumas 2019	US	2009-2015	Workforce-based prospective cohort study (NHSII)	73,262 female registered nurses	Questionnaires	Age, smoking status and pack-years, race, ethnicity, and BMI	Highest exposure level to disinfectants, and sprays	Incident physician-diagnosed COPD Weekly use of any disinfectant: HR=1.35 (1.14-1.59) Weekly use of sprays: HR=1.27 (0.97-1.66)	High
Lung function and other health outcomes									
Zock 2002	11 European countries and 3 outside Europe	1990-1994	Population-based survey (ECRHS)	82 cleaners, 543 office workers	Spirometry, methacholine challenge test	Age, gender, smoking, study centre	Cleaning occupation	Not significantly associated with changes in FEV1, FVC or FEV1/FVC but was significantly associated with a decrease in PEF ($p<0.05$) Lower atopy in cleaners compared to office workers (38.3% vs. 60.9%; $p<0.05$)	High
Medina-Ramon 2005	Spain	2000-2001	Case-control, nested within a large population-based survey	Domestic cleaning women, 40 cases (with asthma and/or chronic bronchitis symptoms, 155 controls)	Questionnaire Lung function, methacholine challenge, serum IgE testing Personal measurements of airborne chlorine and ammonia	Age, smoking, bleach, cleaning products, washing dishes, inhalation accidents, non-domestic cleaning	Female domestic cleaners	No difference between cases and controls with regards to FEV1	Moderate
Corradi 2012	Italy	Not specified	Workforce-based cross-sectional	40 hospital cleaners, 40 controls	Spirometry	Age, gender, ethnicity, height	Hospital cleaners	Predicted FEV1%: similar in cleaners and controls. No difference in FeNO among cleaners compared to controls.	Moderate

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Vizcaya 2013	Spain	2008-2009	Workforce-based case-control nested in a cross-sectional study among cleaning company employees	42 asthma cases, 53 controls	Spirometry during clinic visit	Age, gender, smoking	Female cleaners	Most irritant products and sprays were more often used by asthmatic cleaners. The use of multiuse products, glass cleaners and polishes at work was associated with higher FeNO, particularly in controls. No differences between cases and controls in levels of FeNO, or biomarkers of oxidative stress.	Moderate
Vizcaya 2015	Spain	2008-2009	Workforce-based cross-sectional panel	21 female cleaners with current asthma	Spirometry	Age, smoking, having a cold or flu, use of respiratory medication	Cleaning agents	FEV1 reduction after exposure to hydrochloric acid, solvents, and sprays among current cleaners with asthma	Low
Casimirri 2016	Italy	Not specified	Workforce-based cross-sectional	40 hospital cleaners, 40 non-exposed controls	Spirometry	Age, smoking, BMI	Chlorinated agents	Higher EBC biomarkers of oxidative stress and inflammation in cleaners.	Moderate
Svanes 2018	Many European countries	1992-1994 (ECRHS I), 1998-2002 (ECRHS II), 2010-2012 (ECRHS III)	Population-based longitudinal study	6,235 subjects ECHRS I and II, 3,804 subjects (ECHRS III)	Spirometry/bronchodilator test	Age, smoking pack-years, BMI, parents' education and SES	Cleaning occupation, cleaning at home, use of sprays and other agents	More rapid FEV1 decline in women cleaning at home (-22.1 ml/yr, p=0.01) and occupational cleaners (-22.4, p=0.03), compared with women not engaged in cleaning (-18.5) More rapid FVC decline in women cleaning at home (-13.1 ml/yr, p=0.02) and occupational cleaners (-15.9, p=0.002), compared with women not engaged in cleaning (-8.8) Cleaning sprays: FEV1 -22.0 ml/yr, p=0.04) Other cleaning agents: FEV1 -22.9 ml/yr, p=0.004)	High

Author, Year	Country	Year of data collection	Study design	Study population	Method of data collection	Co-variates	Type of exposure	Findings (95% confidence interval in parenthesis)	GRADE score
Brooks 2020	New Zealand	2008-2010	Workforce based cross-sectional	425 cleaners, 281 reference workers	Questionnaires, bronchodilator	Age, gender, ethnicity, smoking	Cleaners	Mean differences between cleaners and referents: FEV1= -0.20 L (−0.29 to-0.10) FEV1 % predicted = -3.12% (−5.68 to-0.57) FVC= -0.25 L (−0.36 to-0.14) FVC % predicted= -3.25% (−5.55 to-0.96)	High

EBC: exhaled breath condensate; ECRHS: European Community Respiratory Health Survey; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; GMR: geometric mean ratio; JEM: job-exposure matrix; LLN: lower-limit of normal; MEF25: maximal expiratory flow at 25% of vital capacity; MEF50: maximal expiratory flow at 50% of vital capacity; OASYS: occupational asthma expert system; OR: odds ratio; PD20: administered cumulative dose of methacholine which results in a drop in FEV1 by 20%; PEF: peak expiratory flow; PR: prevalence ratio

Figure 1 PRISMA flow diagram showing screening and selection of articles related to occupational cleaning and health outcomes resulting from the search in electronic bibliographic databases.

Figure 2 Meta-analysis of 21 studies evaluating the association between occupational cleaning exposure and asthma risk.

Footnote: RR= Relative Risk; CIs= Confidence Intervals.

Figure 3 Meta-analysis of three studies evaluating the association between occupational cleaning exposure and chronic obstructive pulmonary disease (COPD) risk.

Footnote: RR= Relative Risk; CIs= Confidence Intervals.

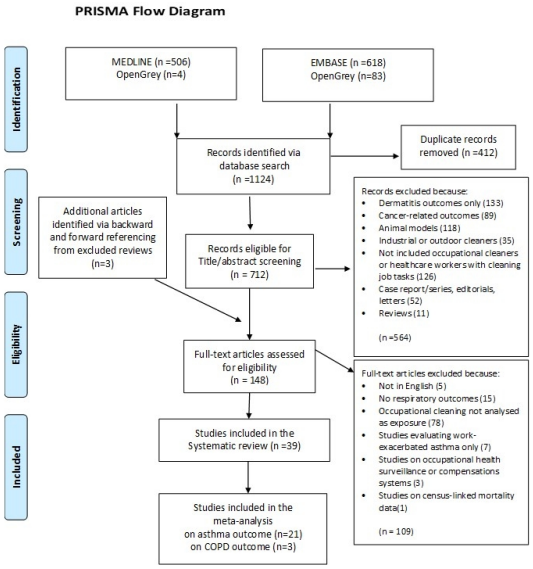

Figure 1 PRISMA flow diagram showing screening and selection of articles related to occupational cleaning and health outcomes resulting from the search in electronic bibliographic databases.

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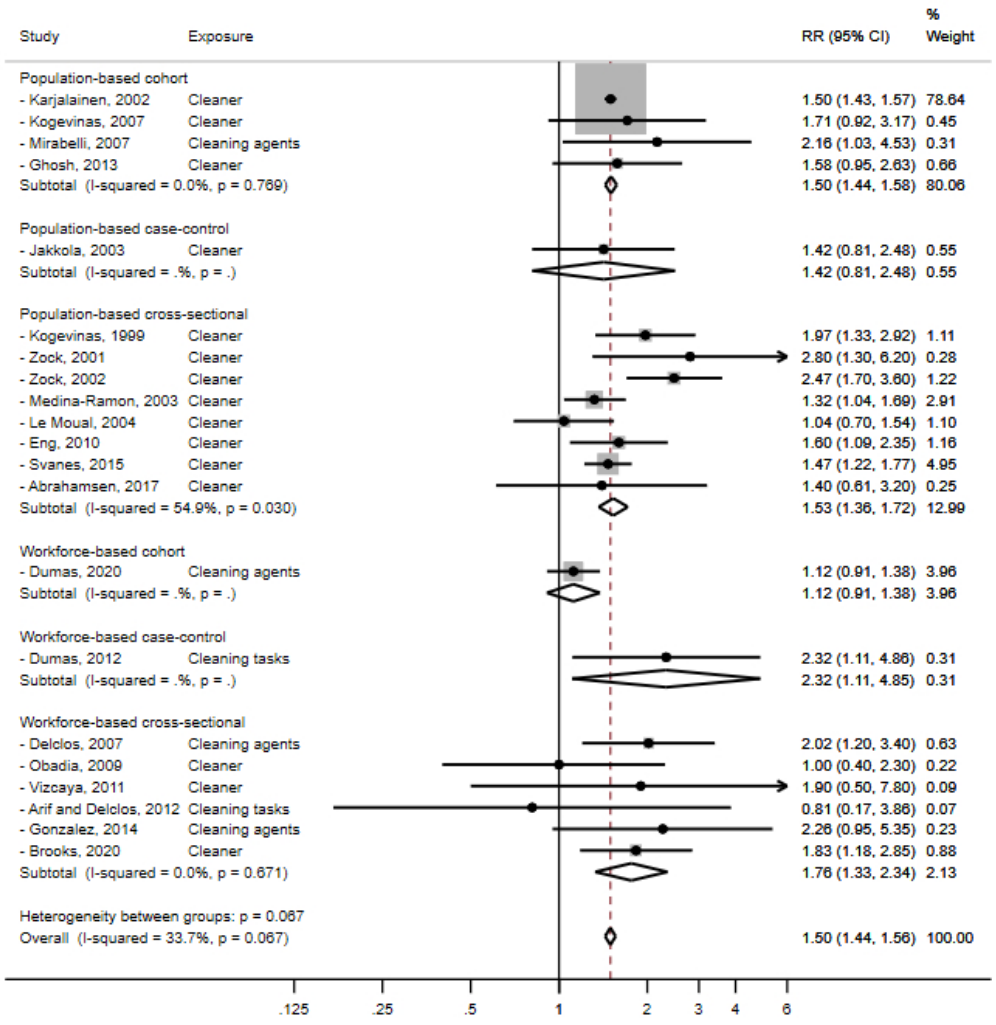


Figure 2 Meta-analysis of 21 studies evaluating the association between occupational cleaning exposure and asthma risk.
Footnote: RR= Relative Risk; CIs= Confidence Intervals.

227x237mm (72 x 72 DPI)

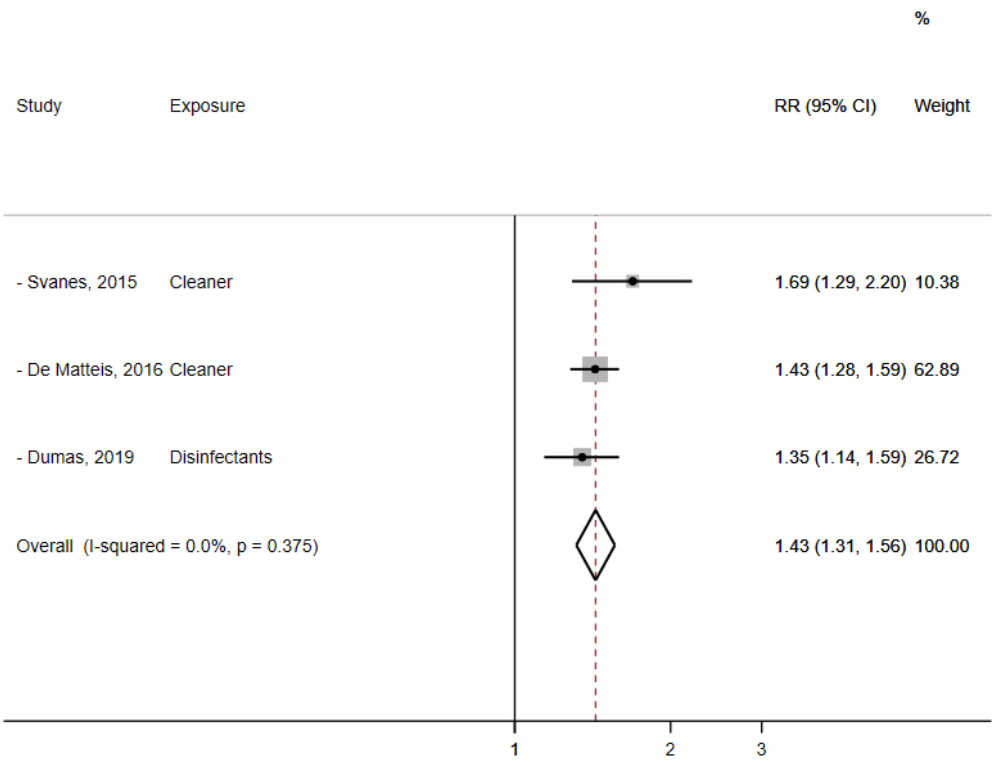


Figure 3 Meta-analysis of three studies evaluating the association between occupational cleaning exposure and chronic obstructive pulmonary disease (COPD) risk.
Footnote: RR= Relative Risk; CIs= Confidence Intervals.

274x237mm (72 x 72 DPI)

SUPPLEMENTARY FILE

Table S1: Search strategy containing the keywords, MeSH terms and Boolean operators used to retrieve references on the MEDLINE (PUBMED) and EMBASE databases

DATABASE	**MEDLINE via PUBMED**
DATE	**24th March 2017 and updated to the 31st July 2020**
STRATEGY	**#1 AND #2 AND #3 AND #4**
#1	Occupation*
#2	Clean*
#3	Detergents [mesh] OR Irritants [mesh] OR Disinfectants [mesh] OR Spray* OR Allergens [mesh] OR Inhalation exposure [mesh] OR Occupational exposure [mesh]
#4	Respiratory tract diseases [mesh] OR Bronchial hyperreactivity [mesh] OR Airway hyper* OR Respiratory hypersensitivity [mesh] OR Airway irritation OR Airway obstruction OR Respiratory symptoms OR Airway symptoms OR Cough [mesh] OR Wheez* OR Dyspnea [mesh] OR Chest tightness OR Lung function OR Forced expiratory volume [mesh] OR Vital capacity [mesh] OR Peak expiratory flow rate [mesh] OR Respiratory function tests [mesh] OR Bronchial provocation tests [mesh] OR FeNO OR Asthma OR Occupational asthma [mesh] OR Occupational disease [mesh] OR Work-related asthma OR Work-exacerbated asthma OR Rhinitis [mesh] OR Pulmonary disease, chronic obstructive [mesh] OR Vocal cord dysfunction [mesh]
DATABASE	**EMBASE**
DATE	**24th March 2017 and updated to the 31st July 2020**
STRATEGY	**#1 AND #2 AND #3 AND #4**
#1	Occupation*
#2	Clean* or Cleaning [mesh]
#3	Detergent [mesh] OR Irritant agent [mesh] OR Disinfectant agent [mesh] OR Spray* OR Allergen [mesh] OR Inhalation exposure [mesh] OR Occupational exposure [mesh]

#4	Respiratory tract disease [mesh] OR Lower respiratory tract [mesh] OR Bronchus hyperreactivity [mesh] OR Airway hyper* OR Airway irritation OR Airway obstruction [mesh] OR Respiratory symptoms OR Airway symptoms OR Coughing [mesh] OR Wheezing [mesh] OR Dyspnea [mesh] OR Chest tightness [mesh] OR Lung function [mesh] OR Forced expiratory volume [mesh] OR Vital capacity [mesh] OR Peak expiratory flow [mesh] OR Respiratory function [mesh] OR Provocation test [mesh] OR Inhalation test [mesh] OR FeNO OR Asthma [mesh] OR Occupational asthma [mesh] OR Occupational disease [mesh] OR Work-related asthma OR Work-exacerbated asthma OR Rhinitis [mesh] OR Chronic obstructive lung disease [mesh] OR Vocal cord disorder [mesh]

Table S2. Inclusion and exclusion criteria used when screening retrieved articles.

Inclusion Criteria	
1	Adults (>18 years old)
2	Professional cleaners (receive a wage to clean) – domestic and non-domestic
3	Healthcare workers including nurses with cleaning job tasks
4	Observational studies
Exclusion Criteria	
1	Cleaners who work in industrial/factory settings or use industrial cleaning products
2	Cleaners who work outdoors
3	Non-professional domestic cleaners
4	Not in English
5	Literature reviews, Editorials, Letters
6	Case reports/series
7	Studies evaluating work-exacerbated asthma only
8	Studies on occupational health surveillance or compensations claim systems
9	Studies on census-linked data

Table S3: Summary of epidemiological studies assessing the associations between professional cleaning work (domestic vs. non-domestic) and asthma and rhinitis. Also low/very low quality studies are included.**Author**	**Year**	**Country**	**Year of data collection**	**Study design**	**Sample size (n)**	**Method of data collection**	**Co-variates**	**Type of cleaner**	**Findings**		**GRADE score**
									Asthma	**Rhinitis**	

Zock et al.	2002	11 European and 3 outside Europe		Population-based cross-sectional	4796	Questionnaire, Blood samples for serum IgE	Age, Gender, Smoking, Study centre		WRA OR 2.47 (95% CI 1.7 – 3.6) Possible mechanism: Cleaning significantly reduces association with atopy OR 0.51 (p<0.05)		Moderate
Karjalainen et al.	2002	Finland	1986-1998	Registry-based cohort	53708 cleaners/ 202751 administrative managerial and clerical workers	The Medication Reimbursement Register of the SII of Finland and the Finnish Register of Occupational Diseases (FROD)	Age, Follow-up period	Female cleaners	WRA RR 1.50 (95% CI 1.48 – 1.57)		High
Jaakkola et al.	2003	Finland		Population-based case-control	521 asthma/ 932 non-manual workers	Questionnaire	Age, Gender, Smoking,	Female cleaners	OA OR 1.42 (95% CI 0.81 - 2.48)		Moderate

Le Moual et al.	2004	France	1975	Population-based cross-sectional	8832	Questionnaire	Age, Gender, Smoking		WRA OR 1.04 (95% CI 0.70 - 1.54)		Moderate
Eng et al.	2010	New Zealand	2004-2006	Population-based cross-sectional	3055	Telephone survey	Age, Gender, Smoking, Deprivation		WRA OR 1.3 (95% CI 0.8 – 2.1)		Moderate
Vizcaya et al.	2011	Spain	2007-2008	Workforce-based cross-sectional study	917	Questionnaire	Age, Gender, Smoking, Nationality		WRA OR 2.1 (95% CI 1.1 - 4.2)		Moderate
Radon et al.	2008	13 countries in Europe	Baseline study: 1991-1995 Follow up: 1998-2003	Prospective population-based cohort	4994	Face to face interview, Skin prick test	Age Gender Smoking Level of smoking Parental allergy Country of residence			Allergic rhinitis in males OR 1.22 (95% CI 0.59 – 2.55) Allergic rhinitis in females OR 1.26 (95% CI 0.81 - 1.95) Perennial rhinitis in males OR 0.99 (95% CI 0.49 - 2.02)	High

										Perennial rhinitis in females OR 1.70 (95% CI 1.09 - 2.64)	
Folleti et al.	2012	Italy		Population-based cross-sectional	297	Questionnaire, Skin prick test	Age, Gender, Smoking, Atopy, Schooling, Cleaning tasks or products		WRA: 7% in cleaners and 1% in controls (p<0.05)	Rhinitis: 17% in cleaners and 15% in controls (p>0.05)	Low
									Possible mechanism: The prevalence of atopy was 30% in cleaners and 48% in controls		
Lipinska-Ojrzanowska et al.	2014	Poland		Population-based cross-sectional	70	Questionnaire			WRA among cleaners was positively associated with rhinitis (p=0.019)		Very low
Svanes et al.	2015	Norway, Sweden, Denmark, Iceland and Estonia	2010-2012	Population-based cross-sectional	13499	Questionnaire	Age, Gender, Smoking, Educational level, Parent's educational level, BMI,	Occupatio-nal cleaner ≤1 year exposure	OA OR 1.47 (95% CI 1.22 – 1.27) OA OR 0.92 (95% CI 0.65 – 1.31)		High

							Participating centre	1-4 years exposure ≥4 years exposure	OA OR 1.44 (95% CI 1.05 – 1.97) OA OR 1.59 (95% CI 1.22 – 2.08)		
Radon et al.	2016	Peru	2011-2013	Population-based cross-sectional	278	Questionnaire	Gender, Smoking, Duration of employment		WRA: 22% in cleaners and 5% in controls (p=0.001)	Allergic rhinitis: 21% in cleaners and 13% in controls (p=0.12)	Moderate

DOMESTIC CLEANERS											
Author	**Year**	**Country**	**Year of data collection**	**Study design**	**Sample size (n)**	**Method of data collection**	**Co-variates**	**Type of cleaner**	**Findings**		**GRADE score**
									Asthma	**Rhinitis**	
Zock et al.	2001	Spain	1992	Population-based cross-sectional	1339	Questionnaire		Private domestic cleaners	WRA PR 3.3 (95% CI 1.9 — 5.8) WRA + BHR PR 5.0 (95% CI 1.9 — 13.2)		Moderate
Medina-Ramon et al.	2003	Spain	2000-2001	Population-based cross-sectional	4521	Questionnaire	Age, Smoking	Current domestic cleaners Former domestic cleaners	WRA OR 1.46 (95% CI 1.10 - 1.92) WRA OR 2.09 (95% CI 1.70 - 2.57)	Work-related rhinitis OR 1.18 (95% CI 0.97 - 1.42) Work-related rhinitis OR 1.31 (95% CI 1.13 - 1.51)	High
Ghosh et al.	2013	Great Britain	1991-2000	Population-based cross-sectional	113	Interview	Gender, Smoking, Father's social class, Area of residence at 42 years, Hayfever/ allergic	Domestic cleaners	WRA OR 1.79 (95% CI 1.02 - 3.14, p=0.044)		Moderate

							rhinitis in childhood				
NON-DOMESTIC CLEANERS											
Author	**Year**	**Country**	**Year of data collection**	**Study design**	**Sample size (n)**	**Method of data collection**	**Co-variates**	**Type of cleaner**	**Findings**		**GRADE score**
									Asthma	**Rhinitis**	
Medina-Ramon et al.	2003	Spain	2000-2001	Population-based cross sectional	4521	Questionnaire	Age, Smoking	Current non-domestic cleaners Former non-domestic cleaners	WRA OR 1.08 (95% CI 0.72-1.61) WRA OR 1.41 (95% CI 0.91-2.18)	Work-related rhinitis OR 0.92 (95% CI 0.71 - 1.20) Work-related rhinitis OR 1.11 (95% CI 0.82 - 1.50)	High

Macaira et al.	2007	Brazil		Population-based cross-sectional	341	Questionnaire, Skin prick test	Age, Gender, Smoking, Atopy, Number of years employment in non-domestic cleaning, Inhalation accidents	0.92-3 years exposure 3-6.5 years exposure >6.5 years exposure	WRA/rhinitis OR 1.09 (95% CI 1.00 - 1.18) WRA/rhinitis OR 1.28 (95% CI 1.01 - 1.63 WRA/rhinitis OR 1.71 (95% CI 1.02 - 2.89 Possible mechanism: Asthma was significantly associated with atopy OR 2.91 (95% CI 1.36 - 6.71)	Rhinitis in females OR 2.07 (95% CI 1.20 - 3.70) compared to males Possible mechanism: Work-related rhinitis was significantly associated with atopy OR 2.06 (95% CI 1.28 - 3.35)	Moderate
Mirabelli et al.	2007	13 European countries	1991, 1998-1999	Prospective population-based cohort	332 nursing and related occupation/ 2481 professional or administrative occupation	Questionnaire	Age, Gender, Smoking	Working in nursing and other healthcare related jobs	OA RR 1.16 (95% CI 0.72 - 1.87)		Moderate

Delclos et al.	2007	USA	2003	Population-based cross-sectional	5387	Questionnaire	Age, Gender, Smoking, Atopy, Ethnicity, Obesity, Seniority (number of years as a HCP)	Healthcare workers 0-9 years exposure 10-16 years exposure 17-26 years exposure ≥27 years exposure	WRA in females OR 2.31 (95% CI 1.35 – 3.94) compared to males WRA OR 1.00 WRA OR 2.08 (95% CI 0.64 – 6.73) WRA OR 3.37 (95% CI 1.10 – 10.26) WRA OR 4.10 (95% CI 1.39 – 12.11)		High
Obadia et al.	2009	Canada		Workforce-based cross-sectional	1153	Questionnaire	Age, Gender, Smoking	School or racetrack public building cleaners	OA in males OR 0.93 (95% CI 0.4 – 2.3) OA in females OR 1.00 (95% CI 0.4 – 2.3)		Moderate

Dumas et al.	2012	France	2003-2007	Population-based case-control	136 hospital workers/ 333 non-exposed subjects	Questionnaire, Expert assessment	Age, Gender, Smoking, BMI	Female hospital workers (healthcare workers/ hospital cleaners)	WRA OR 1.14 (95% CI 0.69 - 1.87)		High
Ghosh et al.	2013	Great Britain	1991-2000	Population-based cross-sectional	516	Interview	Gender, Smoking, Father's social class, Area of residence at 42 years, Hayfever/ allergic rhinitis in childhood	Office and hotel cleaners	WRA OR 1.82 (95% CI 1.34 - 2.48, p<0.001)		Moderate
Gonzalez et al.	2014	France	2006-2007	Workforce-based cross-sectional	153	Questionnaire	Age, Gender, Smoking, Atopy, BMI	Hospital cleaners	WRA OR 2.38 (95% CI 0.48 - 11.85) OA OR 2.33 (95% CI 0.52 - 10.44)		Moderate

OR: Odds Ratio, CI: Confidence Interval, RR: Relative Risk, WRA: Work-related asthma, OA: Occupational Asthma

Table S4: Summary of epidemiological studies assessing the associations between professional cleaning work and lung function, and bronchial hyperresponsiveness (BHR). Also low/very low quality studies are included.

Author	Year	Country	Year of data collection	Study design	Sample size (n)	Method of data collection	Co-variates	Type of cleaner	Findings		GRADE score
									Lung function	BHR	
Zock et al.	2002	11 European and 3 outside Europe		Population-based cross-sectional	4796	Spirometry, Methacholine challenge test	Age, Gender, Smoking, Study centre		Not significantly associated with changes in FEV_1, FVC or FEV_1/FVC but was significantly associated with a decrease in PEF ($p<0.05$)	No significant association OR 1.60 ($p>0.05$)	Moderate
Medina-Ramon et al.	2005	Spain	2000-2001	Nested case-control	40 case/ 155 controls	Spirometry, Methacholine challenge test	Age, Smoking, Cleaning tasks and products, Current or former employment in non-domestic cleaning jobs, History/ inhalation accidents relating to cleaning products	Female domestic cleaners	No significant difference between cases and controls with regards to FEV_1	Large difference in the rates of BHR (18% versus 3%) between cases and controls	Moderate

Karadzinska-Bislimovska et al.	2007	Macedonia	2004-2006	Population-based cross-sectional	88	Histamine challenge test	Smoking, BMI, Baseline FEV1	Female cleaners		Prevalence of BHR was higher in cleaners than controls though not significant (30.2% vs 17.7%). Prevalence of borderline BHR was significantly higher in cleaners than controls (16.2% vs 6.6%, p=0.032)	Low
Makela et al.	2011	Finland	1994-2004	Registry-based cross-sectional	20	Spirometry		Female cleaners	Flow-volume spirometry was normal in 12 subjects and there was mild deterioration in the remaining 8 subjects		Low
Corradi et al.	2012	Italy		Workforce-based cross-sectional	80	Spirometry	Age, Gender, Ethnicity, Height	Hospital cleaners	Cleaners had spirometry results within the normal range after adjustment		Moderate

Vizcaya et al.	2013	Spain	2008-2009	Nested case-control	42 cases/ 53 controls	Spirometry during detailed clinic visit	Age, Gender, Smoking		Pre- and post-bronchodilator FEV_1/FVC ratios were significantly lower in cases compared to controls. OR −4.4 (95% CI −7.4 to −1.5) and OR −5.2 (−8.8 to −1.6), respectively.		Moderate
Ghosh et al.	2013	Great Britain	1991-2000	Population-based cross-sectional	516	Spirometry, Interview	Gender, Smoking, Father's social class, Area of residence at 42 years, Hayfever/ allergic rhinitis in childhood	Office and hotel cleaners	Airflow limitation with adult-onset asthma OR 2.25 (95% CI 1.19 - 4.24, p=0.012)		Moderate
Vizcaya et al.	2015	Spain	2008-2009	Workforce-based cross-sectional	21	Spirometry	Age, Smoking, Having a cold or flu, Use of respiratory medication	Female cleaners	FEV_1 evening following exposure: −86ml (95% CI −212 to 39) FEV_1 morning following exposure: −50ml (95% CI −181 to 81) Diurnal variation in FEV_1: 2.8ml		Low

									(95% CI −1.0 to 6.6)		
Casimirri et al.	2016	Italy		Workforce-based cross-sectional	78	Spirometry	Age, Smoking, BMI,	Caucasian female hospital cleaners	No significant association between cleaning and FEV_1, FVC (% predicted) and the FEV_1/FVC ratio		Moderate

OR: Odds Ratio; GMR: Geometric mean ratio; CI: Confidence Interval; PEF: Peak Expiratory Flow; MEF25: Maximal Expiratory Flow at 25% of vital capacity; MEF50: Maximal expiratory flow at 50% of vital capacity; FEV1:Forced Expiratory Volume in one second; FVC: Forced Vital Capacity; OASYS – Occupational asthma expert system; PD20: Administered cumulative dose of methacholine which results in a drop in FEV1 by 20%

Table S5: Summary of epidemiological studies assessing the association between professional cleaning work and upper respiratory symptoms and lower respiratory symptoms. Also low/very low quality studies are included.

Author	Year	Country	Year of data collection	Study design	Sample size (n)	Method of data collection	Co-variates	Type of cleaner	Findings		GRADE score
									URTSs	LRTSs	
Medina-Ramon et al.	2006	Spain	2001-2002	Population-based cross-sectional	43	Questionnaire	Age, Smoking, Respiratory infections, Maintenance medications, Exposure period	Female domestic cleaners	URTSs not significantly associated with the working day OR 1.1 (95% CI 0.6 – 2.3)	LRTSs significantly associated with the working day OR 3.1 (95% CI 1.4 – 7.1)	Moderate
Karadzinska-Bislimovska et al.	2007	Macedonia	2004-2006	Population-based cross-sectional	88	Questionnaire	Smoking, BMI, Baseline FEV1	Female cleaners		Significantly higher prevalence of phlegm (p=0.019) and dyspnoea (p=0.041) in cleaners compared to the control group	Low

Declos et al.	2007	USA	2003	Population-based cross-sectional	3650	Questionnaire	Age, Gender, Smoking, Atopy, Obesity (BMI>30kg/m2), Seniority (number of years as a HCP)	Nurses	BHR-related symptoms[a] OR 1.95 (95% CI 1.51–2.52)	High
Obadia et al.	2009	Canada		Workforce-based cross-sectional	1153	Questionnaire	Age, Gender, Smoking	School or racetrack public building cleaners	Prevalence of LRTSs in females OR 2.59 (95% CI 1.6 - 4.3) Prevalence of LRTSs in males OR 1.16 (95% CI 0.7 – 1.9)	Moderate
Wiesland er et al.	2010	Sweden		Population-based cross-sectional	21	Questionnaire		Hospital cleaners	Significant increase in nasal symptoms ($p<0.001$) and throat symptoms ($p<0.05$) Significant increase in dyspnoea ($p<0.01$)	Low
Vizcaya et al.	2011	Spain	2007-2008	Workforce-based cross-sectional study	831	Questionnaire	Age, Gender, Smoking, Nationality		Wheeze without having a cold OR 1.3 (95% CI 0.5 - 3.3) Chronic cough OR 1.8 (95% CI 0.7 - 4.7)	Moderate
Lipinska-Ojrzanowska et al.	2011			Population-based cross-sectional	103	Questionnaire			29.1% subjects reported rhinitis symptoms 26.2% subjects reported dyspnoea symptoms and 14.6% reported chronic cough symptoms	Very low

Corradi et al.	2012	Italy		Workforce-based cross-sectional	80	Questionnaire	Age, Gender,	Hospital cleaners	Most frequently reported symptoms in cleaners were sneezing (27.5%), nasal and/or pharyngeal itch (25%) and ocular itch (22.5%). No significant difference in symptoms between cleaners and the control group	22.5% of cleaners reported cough. No significant difference in symptoms between cleaners and the control group	Moderate
Lipinska-Ojrzanowska et al.	2014	Poland		Population-based cross-sectional	70	Questionnaire			Cleaners suffered mainly from cough (84%)		Very low
Gonzalez et al.	2014	France	2006-2007	Workforce-based cross-sectional	153	Questionnaire	Age, Gender, Smoking, Atopy, BMI	Hospital cleaners	Nasal symptoms OR 1.73 (95% CI 0.89 - 3.34)		Moderate
Lee et al.	2014	USA		Workforce-based cross-sectional	183	Questionnaire, Face to face interview	Age, Gender, Job title	Hospital cleaners	Respiratory symptoms OR 1.01 (95% CI 0.40 – 2.50) High		

									Stuffy, itchy or runny nose (19%) was the most common respiratory symptom	
Lipinska-Ojrzanowska et al.	2014	Poland		Workforce-based cross-sectional	142	Questionnaire		Health centre cleaners	Nasal (rhinitis) symptoms (34.5%) were the most common Dyspnoea was present in 25.4% of subjects and cough in 24.0% subjects	Low
Svanes et al.	2015	Norway, Sweden, Denmark, Iceland and Estonia	2010-2012	Population-based cross-sectional	13499	Questionnaire	Age, Gender, Smoking, Educational, level, Parent's educational level, BMI, Participating centre		Risk of wheeze in ever-cleaners OR 1.44 (95% CI 1.27 –1.62) Asthma symptoms OR 1.66 (95% CI 1.46 – 1.90)	High
Felix et al.	2016			Population-based cross-sectional	167	Questionnaire		Hospital cleaners (G1) University cleaners (G2) Domestic cleaners (G3)	Rhinitis symptoms (G1- 46%, G2-25%, G3-29%). Controls presented with no respiratory symptoms Asthma symptoms (G1-43%, G2-57%). Controls presented with no respiratory symptoms	Very low

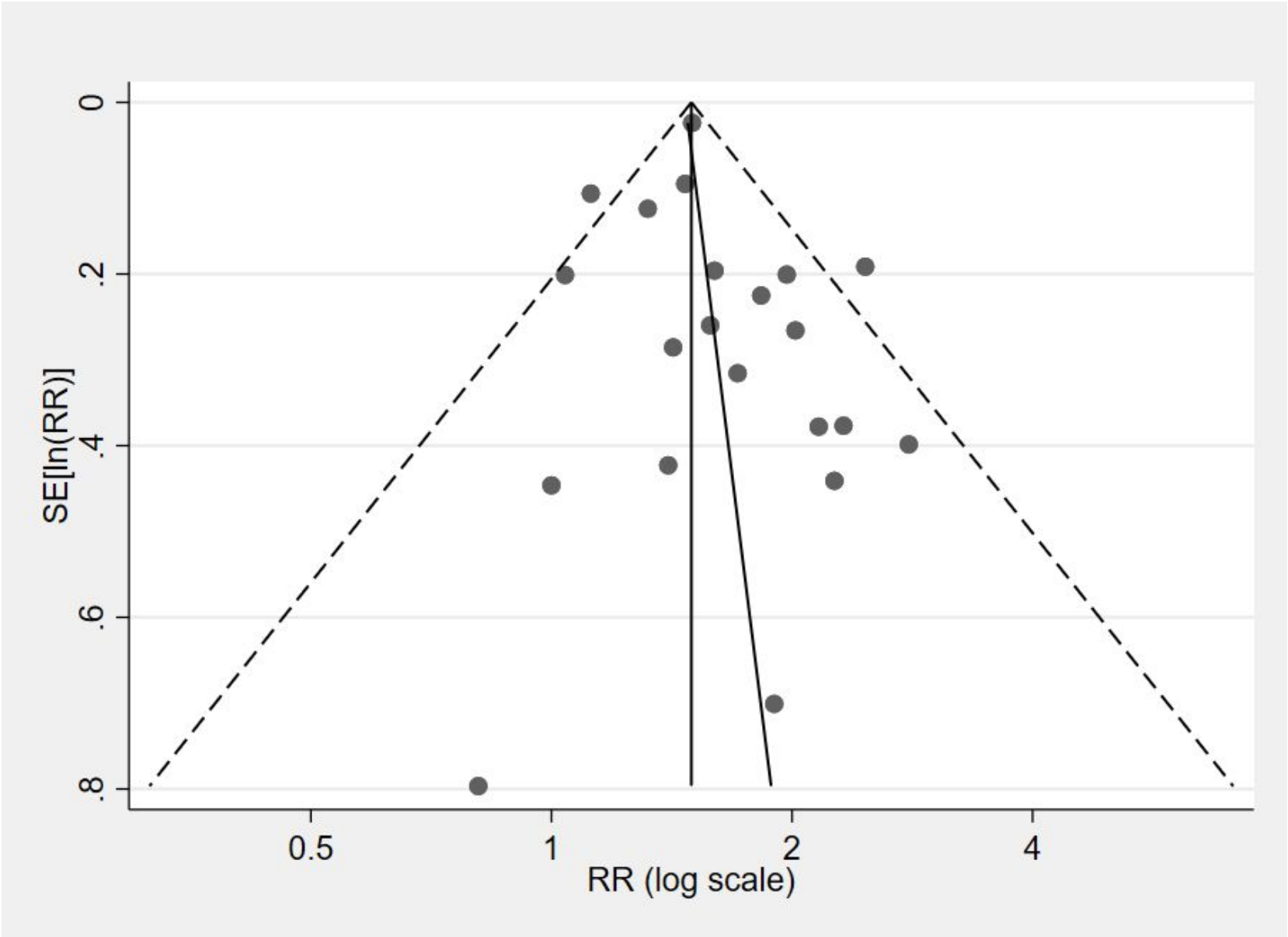
Casimirri et al.	2016	Italy		Workforce-based cross-sectional	80	Questionnaire	Age, Smoking, BMI,	Caucasian female hospital cleaners	No significant difference in symptoms between cleaners and administrative employees	Moderate
Fell et al.	2016	Norway	2013	Longitudinal case-control	247 cases/ 15,655 controls	Questionnaire	Age, Gender, Smoking		Job change due to respiratory symptoms OR 5.0 (95% CI 2.2 - 11)	Low
Lipinska-Ojrzanowska et al.	2017	Poland		Population-based cross-sectional	50	Questionnaire		Female cleaners	No significant difference in respiratory symptoms in cleaners with or without asthma	Moderate

BHR-related symptoms based on the following eight factors: trouble breathing, wheezing and/or attacks of shortness of breath in the previous 12 months, nocturnal cough and/or chest tightness in the previous 12 months and current allergic symptoms when in the presence of animals, feathers, dust, trees, grasses, flowers, or pollen. OR: Odds Ratio; CI: Confidence Interval; URTSs: Upper Respiratory Tract Symptoms; LRTSs: Lower Respiratory Tract Rymptoms.

Table S6. Summary of epidemiological studies assessing the associations between professional cleaning work and respiratory health effects retrieved via OpenGrey.

Author, Year	Country	Year of data collection	Study design	Sample size (n)	Method of data collection	Co-variates	Type of exposure	Findings	GRADE score
Nasir 2011 (Abstract)	UK	Not available	Workforce-based Cross-sectional survey	216 cleaners, 645 administrative staff	Questionnaires	Age	Hospital cleaners	current asthma OR =1.21, 95% CI: 0.77-1.84) chronic bronchitis (OR=1.52, 95% CI 0.98 to 2.33)	Very Low
Mijakoski et al. 2013 (Abstract)	FYROM	Not available	Population-based case-control	100 cleaners	Spirometry, Histamine challenge test	None	Female cleaners	Female cleaners had a higher prevalence of BHR vs. office workers ($p<0.05$), and lower MEF25 ($p<0.025$), and MEF50 ($p<0.05$). More respiratory symptoms (36% vs 16%, $p<0.05$): cough (38% vs 14%, $p<0.05$), shortness of breath (40% vs 18%, $p<0.05$)	Very Low

Alfajjam et al. 2012 (PhD thesis)	UK	2012	Workforce-based cross-sectional survey	13	Spirometry, Methacholine challenge test	Age, gender	Cleaners in hospital trusts and universities	Only one subject had an OASYS score of > 2.5 indicative of occupational asthma. The mean OASYS score was 1.97. Mean PD20 at work was 193µg and away from work mean PD20 was 254µg (p=0.5)	Very low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0
.2
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1
2
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RR (log scale)

Figure S1 Funnel plot including 21 studies pooled in the meta-analysis for asthma outcome to assess publication bias.

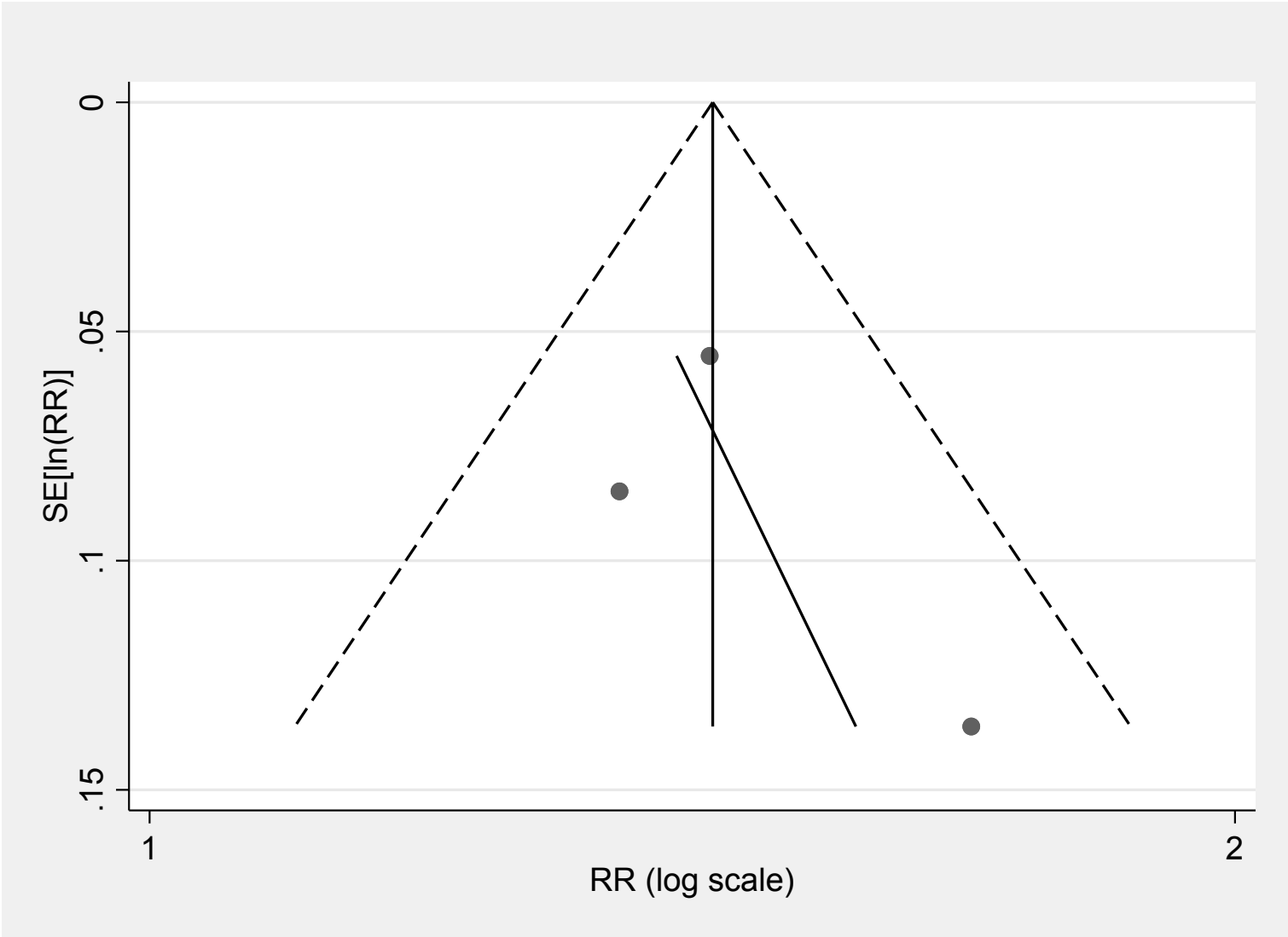
0
.05
.1
.15
SE[ln(RR)]
1
2
RR (log scale)

Figure S2 Funnel plot including three studies pooled in the meta-analysis for chronic obstructive pulmonary disease (COPD) outcome to assess publication bias.